

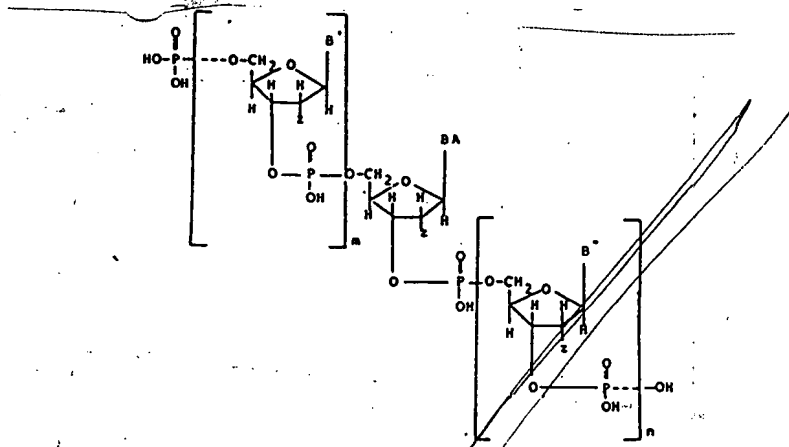
106. (amended) ~~[[A] The method [in accordance with] of claim 104 wherein said polypeptide [comprises] is selected from the group consisting of avidin, streptavidin, and [rabbit IgG] anti-A immunoglobulin.~~

107. (amended) ~~[A] The method [in accordance with] of claim 104 wherein [the moiety] A [of said compound] is a hapten and said polypeptide is an antibody thereto.~~

108. (amended) ~~[A] The method [in accordance with] of claim 104 wherein [the moiety] A [of said compound] is a ligand.~~

109. (amended) ~~[A] The method [in accordance with] of claim 104 wherein the moiety included [in] with said polypeptide which can be detected is [a] fluorescent [dye], electron dense [protein], or is an enzyme capable of [depositing an insoluble] reacting with a substrate to form a detectable reaction product.~~

125. (amended) A method of determining the presence or absence of a target in a sample [of a deoxyribonucleic or ribonucleic acid molecule] which comprises [forming a double-stranded hybrid polynucleotide duplex which includes a single strand of deoxyribonucleic or ribonucleic acid corresponding to or derived from said deoxyribonucleic or ribonucleic acid molecule and a] contacting said sample with at least one compound [in accordance with claim 47] having the structure:



wherein each of B, B', and B'' represents a purine, deazapurine, or pyrimidine moiety covalently bonded to the C^{1'}-position of the sugar moiety, provided that whenever B, B', or B'' is purine or deazapurine, it is attached at the N⁹-position of the purine or deazapurine, and whenever B, B', or B'' is pyrimidine, it is attached at the N¹-position;

wherein A represents at least one component of a signalling moiety and consists of at least three carbon atoms;

wherein B and A are attached directly or through a linkage group, said linkage group not interfering substantially with the characteristic ability of B to hybridize with said target or of A to produce a detectable signal wherein if B is purine A is attached to the 8-position thereof, if B is deazapurine A is attached to the 7-position thereof, and if B is deazapurine A is attached to the 7-position thereof, and if B is pyrimidine A is attached to the 5-position thereof; and

wherein Z represents H- or HO-; and

detecting any signal associated with target-bound compounds [said double-stranded hybrid polynucleotide duplex according to the method of Claim 113].

126. (amended) [A] The method [in accordance with] of claim 125 wherein said [deoxribonucleic or ribonucleic acid molecule] target is a nucleic acid sequence derived from a living organism.

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127. (amended) [A] The method [in accordance with]
of claim [125] 126 wherein said living organism [comprises
bacteria, fungi, viruses, yeast and mammals] is selected from
the group consisting of prokaryotes and eukaryotes.

128. (amended) The [A] method of [diagnosing the
presence of a nucleic acid] claim 125 wherein said sample is
suspected of containing an etiological agent [in a subject
which comprises obtaining a suitable sample from said subject,
determining the presence in said sample of deoxyribonucleic or
ribonucleic acid naturally associated with said etiological
agent by forming a double-stranded polynucleotide duplex which
includes a compound in accordance with Claim 47 and a single
strand of deoxyribonucleic or ribonucleic acid corresponding
to or derived from said deoxyribonucleic or ribonucleic acid
which] and said target nucleic acid sequence is naturally
associated with said etiological agent [under suitable
conditions, and detecting the presence of said double-stranded
polynucleotide duplex using the method of Claim 113].

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129. (amended) [A] The method [in accordance with]
of claim 128 wherein said [subject] sample is of human or animal
origin and said etiological agent [includes] is selected from
the group consisting of bacteria, viruses and fungi.

130. (amended) [A] The method of [testing] claim 125
wherein said sample comprises a bacterium [to determine the
presence of] suspected of containing a target nucleic acid
sequence which imparts resistance to an antibiotic [which]
wherein said compound comprises [preparing] a polynucleotide
complementary to the [deoxyribonucleic acid gene] sequence of
said bacterium which confers resistance to said antibiotic [and
includes the compound of Claim 1 incorporated therein, contacting
said polynucleotide with deoxyribonucleic acid obtained from

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said bacterium under suitable conditions so as to form a double-stranded hybrid duplex, contacting said duplex with a polypeptide capable of forming a complex with said hybrid duplex under suitable conditions, said polypeptide including a moiety which can be detected if said complex is formed, and detecting the presence of said complex indicating resistance to said antibiotic and the absence of said complex indicating susceptibility to said antibiotic].

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131. (amended) [A] The method [in accordance with] of claim 130 wherein said ~~bacterium~~^{microorganism} is Streptococcus pyogenes or [Neisseris] Neisseria meningitidis and said antibiotic is penicillin.

132. (amended) [A] The method [in accordance with] of claim 130 wherein said ~~bacterium~~^{microorganism} is Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Streptococcus pyogenes, or Neisseria gonorrhoeae and said antibiotic is a tetracycline.

133. (amended) [A] The method [in accordance with] of claim 130 wherein said ~~bacterium~~^{microorganism} is Mycobacterium tuberculosis and said antibiotic is an aminoglycoside.

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134. (amended) [A] The method of [diagnosing] claim 125 wherein said sample is suspected of containing a target nucleic acid sequence associated with a genetic disorder [in a subject which] and wherein said compound comprises [preparing] a polynucleotide complementary to the [deoxyribonucleic acid gene] sequence [of said subject which is] associated with said genetic disorder [and includes the compound of Claim 1 incorporated therein, contacting said polynucleotide with deoxyribonucleic acid obtained from said subject under suitable conditions so as to form a double-stranded hybrid duplex, contacting said duplex with a polypeptide capable of forming a

complex with said hybrid duplex, said polypeptide including a moiety which can be detected when said complex is formed, and detecting the presence of said complex using an appropriate detection technique, the presence or absence of said complex indicating the presence or absence of said genetic disorder].

135. (amended) [A] The method of [diagnosing] claim 125 wherein said sample is suspected of containing a target nucleic acid sequence associated with thalassemia [in a human subject which] and wherein said compound comprises [preparing] a polynucleotide complementary to the [deoxyribonucleic acid gene] sequence which is absent in thalassemic subjects [and includes the compound of Claim 1 incorporated therein, contacting said polynucleotide with deoxyribonucleic acid obtained from said subject under suitable conditions so as to form a double-stranded hybrid duplex, contacting said duplex with a polypeptide capable of forming a complex with said hybrid duplex under suitable conditions, said polypeptide including a moiety which can be detected when said complex is formed, and detecting the presence of said complex using an appropriate detection technique, the absence of said complex indicating the presence of thalassemia].

136. (amended) [A] The method of claim 125 for chromosomal karyotyping which comprises contacting said sample with [preparing] a series of [modified polynucleotides corresponding] said compounds which are complementary to a series of known genetic sequences located on chromosomes [said polynucleotides including compounds in accordance with Claim 1, contacting said polynucleotides with deoxyribonucleic acid obtained from chromosomes so as to form hybrid duplexes, contacting each of said duplexes with a polypeptide which is capable of forming a complex with each such duplex, said polypeptides including moieties

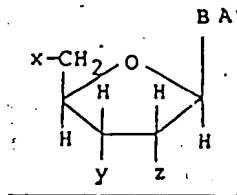
which can be detected when said complexes are formed, and determining the location of each complex on said chromosomes so as to thereby determine the location of said genetic sequences on said chromosomes].

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137. (amended) [A] The method of [detecting a]
claim 125 wherein said sample is suspected of containing a
target polynucleotide which includes [the] a terminal [poly A]
polynucleotide sequence poly A [preparing] and wherein said
compound comprises a modified poly U [molecule] nucleotide
sequence in which at least one uracil moiety has been modified
by chemical addition at the 5' position of [a moiety] A [con-
sisting of at least three carbon atoms which is capable of
forming a detectable complex with a polypeptide when the modi-
fied uracil moiety is incorporated into a double-stranded poly
A-poly U duplex, forming such a poly A poly U duplex by contact-
ing said polynucleotide containing said poly A sequence with
said modified poly U molecule under suitable conditions, and
detecting resulting duplexes so as to thereby detect said poly-
nucleotide].

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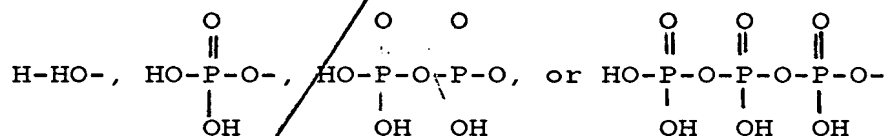
140. (amended) [A] The method of claim 125 wherein
said sample is suspected of containing cells having hormone
receptor sites on the surfaces thereof [of cells] which com-
prises [binding a] contacting said sample with said compound
[in accordance with claim 138 or 139 to the said sites under
suitable conditions permitting binding] having the structure:



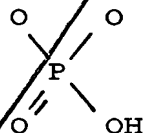
~~wherein B represents a purine, deazapurine, or pyrimidine moiety covalently bonded to the C^{1'}-position of the sugar moiety, provided that when B is purine or deazapurine, it is attached at the N⁹-position of the purine or deazapurine, and when B is pyrimidine, it is attached at the N¹-position; wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic or deoxyribonucleic acid duplex;~~

~~wherein B and A are attached together directly or through a linkage group, said linkage group not interfering substantially with the characteristic ability of A to form a detectable complex with said polypeptide;~~

~~wherein if B is purine, the linkage is attached to the 8 -position of the purine, if B is deazapurine, the linkage is attached to the 7 -position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5 -position of the pyrimidine, and wherein each of x, y and z represents~~



~~and in which x or z is H- or HO- and x and y are reacted to form cyclic moiety for the cyclic moiety.~~



~~disrupting said cells to produce cell surface fragments to which said compound is bound, separately recovering said cell surface fragment, and identifying the same so as to identify said hormone receptor sites.~~

141. (amended) [A] The method of [tumor or cancer cell identification] claim 140 which comprises detecting malignant cells by detecting abnormal hormonal receptor sites associated therewith [according to the method of claim 140].

142. (amended) [A] The method of diagnosing claim 125 wherein said sample is suspected of containing a tumor cell which comprises [preparing] a polynucleotide specific thereto which comprises disrupting said cell and contacting said so-disrupted cell with said compound comprising a sequence which is complementary to a deoxyribonucleic acid gene¹ sequence associated with [production of a polypeptide diagnostic for] said tumor cell [and includes a compound in accordance with claim 1, introducing said polynucleotide into said cell under suitable conditions so as to permit said polynucleotide to hybridize with said deoxyribonucleic acid gene sequence, and determining whether said polynucleotide hybridizes].

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143. (amended) [A] The method [in accordance with] ⁴¹ of claim 142 wherein said polypeptide is α -fetal protein.

144. (amended) [A] The method [in accordance with] of claim 142 wherein said polypeptide is carcinoembryonic antigen.

REMARKS

The above amendments have been made to simplify and to more particularly recite the modified nucleotides and polynucleotides of this divisional application.

Support for claim 104 appears at page 8, lines 18-26. Support for claim 105 appears at page 6, line 3. Support for claim 106 appears at page 27, lines 32 and 33, and at page 28, lines 22-32. Support for claims 107 and 108 appears at page 12, lines 6-9. Support for claim 109 appears at page 28, lines 2-7. Support for claim 125 appears at pages 25